Scylla and the Charybdis between which human society must pick its devious way.

Both are evil. Of the two, monopoly may be the lesser: it may be more easily brought under control; it tends to be more progressive; it extends less far; it may be the less hateful. They are only two expressions of one thing, one possibly worse than the other. Probably there are peoples who pride themselves on more or less complete escape from monopoly who are nevertheless suffering from the most deadening bureaucracy—the insistence on mere governmental accuracy and efficiency.

Agriculture is in the foundation of the political, economic and social structure. If we can not develop starting-power in the background people, we can not maintain it elsewhere. The greatness of all this rural work is to lie in the results and not in the methods that absorb so much of our energy. If agriculture can not be democratic, then there is no democracy.

L. H. Bailey

Microbial Associations[1]

Sociology, as it is generally conceived, conveys a knowledge of the human as a social and ethical creature and maintains for him an harmonious relation to his social environment, as well as considers human society in its ensemble. As an individual, man's composite is different from what it is as a social factor. His attitude toward self is not his attitude toward society at large. Perhaps primitive man was concerned with self only, but with the development of society this limitation was not possible. Man, as he at present exists, has multiplied his individual and social functions. He has developed highly ethical relationships. Under existing conditions, too, he would be wholly helpless without his social ties.

To the biologist, this situation with man, aside from his ethical nature, may be regarded in large measure as material, biological, and may be pertinently designated as special functional development. To the human sociologist, however, the avenue of approach is through the human as a transcendent being in possession of other characteristics than material, and in no sense an animal, but a creature divested of brutish instincts. The spiritual is given command over material functioning. Biological materialism apparently yields to the enshrouding and directing forces of humanism or human ethics. Notwithstanding, the biologist feels and beholds as such a sociology of plants and animals that is very similar, and, furthermore, he sees written in their histories and associations most of the directive agencies operative in human society, only with less ethical exaltation.

This larger sociology, for such it is if we study human sociology biologically as well as through its superficial subjective manifestations, has much interest which is of useful significance. It would not be so difficult to establish parallelisms and expressions of man as an animal in every field of biology, if that were our object. This would, moreover, be a comparative study which can not occupy our attention, for it would lead us far from our purposes. The microbial world, our own province of study, offers itself for specific consideration and is of peculiar and paramount interest to a microbiologist. The possible extensive field of biological sociology just hinted at is used rather to open our minds for the possibilities contained therein.

The microbe, by itself or in pure culture, is only one phase of its existence. In company with other species quite another phase is presented, and this is determined by the associated species and by the many conditions under which these associations may be

[1] Address of the president, Society of American Bacteriologists.

found. Variations and multiplications in functions instituted by these associations, with the resulting products, must influence in the course of time the actual nature of the organism. Its morphology, culture and physiology must assume new aspects, for this accords, by analogy, with recognized laws of environment. If the highly developed molecular, protoplasmic complex is sensitized, some fractional group or radical thereof must yield its claim to some other of superior affinity, which in turn will manifest its presence in all probability either morphologically, culturally or functionally.

Therefore, to suggest merely the richness of a human sociology, a sociology of plants and of animals, and a sociology of microorganisms in a parallelism, fits the mind for the reception of the general principles involved and their projections into the larger field. It prepares the listener to read in fullness between the lines unwritten developments and unwritten biological laws expressed and observed in all living forms.

Humanists rightly call the social treatment sociology, but were we to mention plant and animal sociology and microbial sociology, too much may be injected for human euphony and it may be misleading. For our purposes, microbial associations are sufficiently inclusive and represent many conditions of living together. This is done advisedly, notwithstanding the common usage of the term "symbiosis," which, according to Minchin, should be applied in a restricted sense to mutual advantages on the part of each symbiont involved. Difficulties are therefore avoided by circumvention.

In Frank's treatment[2] of the biological relationships his attitude is clearly revealed by his approach and classification. His parasite depends upon another for nutrition, but the other relationships as the ivy and tree, and the mite and its hosts, as well as De Bary's[3] fungus and alga in mycetozoa, indicate only some of the more apparent biological associations. They record observations without knowledge and demonstration, without research and logical deductions. They are of the order which rank among pioneer scientific effort. Like superficial surveys, they were simply seen and recorded and have been the means of making it possible for a historical, consecutive development. Frank admitted a classification, but, laboring as he did in ignorance of the many facts which have come to light since his time, his classification seems impertinent. Others even later than this, as De Bary, Hansen, Wortmann and Berlise, would have included insects in the carrying of pollen from flower to flower, or yeasts in the starting of fermentation changes, as types of distinctive association.

Probably the first tangible knowledge of *microbial associations* may be traced to Pasteur. It may be that this "Parent of Microbiology" was not fully conscious of the significance of associations, although his work with anaerobic organisms, acetic organisms and brewing organisms must have conveyed an impression which made his mind receptive to other possibilities. There was an inference apparent in nearly all the early work—that some single species was wholly responsible for every recognized process of fermentation or disease. The emphasis thus given to pure cultures has doubtless been the means of minimizing the force and importance of mixed cultures; for has it not been a common experience of workers to witness persistent efforts in securing results by means of pure cultures

[2] A. B. Frank, *Beit. z. Biol. d. Pflanz.*, Bd. 2, S. 123, 1879.

[3] De Bary, "Comp. Morp. and Biol. of Mycetozoa and Bacteria."

from processes which were wholly complex and dependent upon an association of organisms? These intimate interrelations of microorganisms have in a degree been overlooked or neglected because of their complexity.

Garré[4] suggested that one organism may prepare the food for another by changing the medium upon which it may be growing. It is true that this had been demonstrated some years before, by Pasteur and others, but had scarcely been approached in this manner. Marshall Ward[5] added to the knowledge of the world by his studies on ginger beer. The results secured penetrated the heart of the matter and made the suspicions and facts regarding associations replete with a new meaning and value. The Japanese "sake," or rice wine, furnished an example of sequence which too extended the horizon of the nature of fermentations. The milk preparations, koumiss, kephir and many others, did not yield readily to pure culture treatment if gauged by the native products, and accordingly forced the notion of mixed cultures.

Such findings in fermentations coupled with ideas which had been advanced by botanists, as Frank, gave to bacteriological association deeper significance than had been anticipated by the earlier workers. Knowledge had progressed from loose associational relationships through the morphological to the functional aspect of association, as hinted by Garré. Now if functional, as nutrition, is to be interpreted in terms of physics and chemistry, then the basis of attack is at once affirmed. Pfeffer[6] intimated some such foundation when he advanced two classes, "Conjunctive Symbiosis," in which the functioning of one is essential to the functioning of the other—parasitism; and "Disjunctive Symbiosis," in which there is more or less independence; nevertheless, this companionship may be favorable or antagonistic. Out of these, there have apparently emerged with some definiteness "symbiosis," "metabiosis" and "antibiosis," terms familiar to every microbiologist, but not open to exact interpretation.

Pfeffer's classification provided an excellent beginning for associational studies. Whether the term "symbiosis" is satisfactory in his classification depends largely upon individual understanding. It has seemed to me that "association" would be better fitted for the place occupied by "symbiosis," and the "symbiosis" be reserved for a subclass in which a very intimate interdependable relationship exists. Apart from this, I shall follow the division of Pfeffer in our discussion.

In an effort to conform to these general classes of Pfeffer's, it is expedient to subdivide for detailed consideration, since the idea of conjunctive association branches into divers paths and disjunctive association may include many loose relationships.

Auto-relationships or those self-associations, as a class of conjunctive associations which arise from growth and multiplication, are peculiarly suggestive, for they are commonly observed in the laboratory. Organisms will flourish and grow within limitations only upon an ordinary medium, and in the natural changes as fermentations and diseases occurring outside of the laboratory, away from artificial influences, the same phenomena are observable. Buchner[7] and Carnot[8] have claimed that the cholera bacillus and tubercle bacillus find more favorable growth in cultures containing

[4] Garré, *Korrespondenzol. f. Schweiz. Aerzte.*, Bd. 17, 1887.

[5] Ward, *Philos. Trans.*, Vol. 50, 1892.

[6] Pfeffer, *Handbuch der Pflanzenphysiologie*, Leipzig, Bd. I., 1897.

[7] Buchner, *München Arztl. Intelligenzbl.*, No. 50, 1885.

[8] Carnot, *Comptes Med. Soc. de Biol.*, p. 765, 1898.

their products. On the other hand, Duclaux[9] believes that an organism becomes less vigorous when its growth is continued upon media in which some of its products exist. Thibaut,[10] LeSage[11] and Nikitinsky,[12] have studied auto-association. Their results however do not lead to the same conclusions, although they are explicable and constant. There is to be found from Thibaut a suggestion that the existence of fermentation products favors growth of yeasts. Penicillium grown on its own culture does not reach fructification, says LeSage. Then, too, Nikitinsky found favoring conditions when molds are cultivated upon media containing their own products. He noticed as well that antagonistic influences are manifested if the media contain certain carbonaceous substances, even stating that in the presence of carbonaceous foods, probably lactic acid, butyric acid and alcohol are at times responsible for stimulation or retardation. Wildier[13] has introduced the "Bios Fraga." Contrary to the views of Pasteur, he claims that minute quantities of yeast will not grow in the medium of yeast ash, ammonium salts and some sugar. He contends that the element introduced by the addition of greater amounts of yeast for inoculable material is required. He also says that it is a substance very soluble in water, dialyzable, difficult to alter or precipitate, and is found no longer after incineration. It is a substance which exists in small quantities and is indispensable. To this is attached a sort of mysticism which would lead one to recognize some hidden guard within the impregnable fortress of life.

In infectious diseases, there are indications of self-curbing or restrictive development. There appear to be some influences acting in the cases of many pathogens. For instance, the organisms which give rise to influenza, whooping cough and measles and others run their courses; they have their rise and reach their maximum stage of development, and then decline in their activity. Others, as tuberculosis and glanders, appear to be accelerated by their extended development in the body. Again, there is the type which may be designated in general by organisms which are transmitted through carriers or are commensals. Whether an organism reacts upon itself through its growth in media which are fermentable, or in the body of an animal where disease is produced, or where the body acts only as a carrier, is it not possible to discern a common functional principle responsible?

Conjunctive association seems also to designate another subclass which, for the time being, may be called "serial association." One species seems to follow upon the heels of another in point of time, and is dependent upon the other for its life and activity. Sometimes these species appear to grow together simultaneously, but in nearly every case the life and activity of the one depends in sequence upon the life and activity of the other. One seems to be the leader and the other the dependent. There are instances, perhaps, where the relationship between the two suggest an interdependence. In this case, both may be leaders and both dependents. I do not know of a case that has been worked out in detail confirming this peculiar relationship, although observation may suggest it. It may be assumed that in such a case products which are favorable to each are

[9] Duclaux, *Traite de Microbiologie*, Paris, I. and III., 1898 et 1900.

[10] Thibaut, *Cent. f. Bakt.*, Ab. II., Bd. 9, S. 743, 1902.

[11] LeSage, *Travaux scientifiques de l'Université de Reimes*, I., p. 171, 1902.

[12] Nikitinsky, *Jahrb. wiss. Bot.*, 1904, Bd. 40, S. 1.

[13] Wildier, *Le Cellule*, T. 18, p. 313, 1901.

simultaneously created. Where one follows the other, relying upon association products, many illustrations are available.

Ammonification in the soil usually asserts that protein material has undergone change, yielding a series of products by the action of specific classes of organisms. It is known that sometimes in this series more than one class of organisms is involved. After ammonia is produced, the common oxidation processes resulting in nitrites and nitrates are effected by two distinct classes. Accordingly, in the disintegration of a protein molecule by microorganisms, there are probably several classes involved in the process, each in consecutive order. All of them are dependent one upon the other in the various steps of the degradation of the molecule. Then again, if we were to consider the reduction of nitrates to nitrites to nitrogen or ammonium, there are two or three other classes, each waiting its turn in the serial change.

The different stages in the ordinary decomposition of milk speak of this same dependence. At first the several types in milk appear to foster the development of the lactic organisms; following in the wake of the lactic organisms are those which neutralize and then those which cause proteolytic changes; and if we were to trace out the reduction of the complex substances to the various simple mineral constituents that may be found in the final product, there would doubtless be other classes, similar to those found in the mineralizing actions of the soil.

In fermentations, too, are well-known examples: the change of apple must to apple wine, from apple wine to vinegar by yeast and acetic bacteria; the production of ginger beer with a specific yeast and specific bacterium; the making of "Sake" from rice by means of a mold and a yeast; as well as other well-known fermentations in nature, all of which confirm how frequently the life of one organism is dependent upon the life of another. Among the pathogens and those organisms associated with the animal body are many striking instances. The many complications illustrate the possibilities of interdependence—sepsis following scarlet fever and typhoid fever, diphtheria and pest; pneumonia following influenza and tuberculosis; gangrene streptococci with certain anaerobic putrefying organisms; pyogenic bacteria and tetanus organisms. We can not be as certain perhaps and as distinctly satisfied as in the fermentations, the nature of which is so well known, that one product follows another and definitely in the order mentioned, but that there is a decided influence manifest can not be gainsaid. When growing together under circumstances of association, the disease is usually aggravated, or one organism appears to pave the way for another. It is a kind of serial relationship which parallels very closely, to say the least, those which we find in fermentations.

This serial dependence is not lost even where host and parasite are concerned. The tick and the cow are indispensable to the piroplasma in the corpuscle; the fly and the antelope to the trypanosoma in sleeping sickness; the mosquito and man to the plasmodium in malaria; the bacterial forms and man to the ameba in his intestines; the rabbit and some outside habitat to the coccidium. The microorganisms involved in these cases are apparently dependent upon the metazoa concerned for their growth and cyclic development, very much as the nitric organisms are dependent upon the products produced by the serial changes in the breaking down of the protein molecules. In these cases in which animals furnish the material for the life of microorganisms, difficulties are found in the determination of the required condi-

tions and immunity factors of the animal, because of the limitations in knowledge. Is it not fair to suppose, however, that this required material may be just as definite, and may occupy in many cases the same relationship to the organism as in the case of fermentation?

Going a little higher in the scale of life for a single illustration, Keeble[14] contributes an interesting study of association in *Convoluta roscoffensis.*

> In its earlier youth *Convoluta roscoffensis* feeds after the manner of animals in general, on other plants and animals. This is the first stage. In the course thereof green cells appear in the body, increase, multiply, photo-synthesize and distribute food material to the animal tissues. For a while, *Convoluta roscoffensis* receives food from two sources—from ingested plants and animals and from its green cells. This second phase is succeeded by a third in which *Convoluta roscoffensis,* having ceased to ingest solid food, is nourished in the same manner as the colorless non-chlorophyllous tissues of a green plant are nourished, by the products of the photosynthetic activity of its green cells. The last stage of all which ends this strange eventful history: The animal digests its green cells, and having done so dies. In the first phase the mode of nutrition is animal-wise; in the second, part animal, part plant-wise; in the third, altogether plant-wise or holophytic, and in the fourth auto-trophic, that is by living on itself.

Interesting cases of animals and plants higher in the scale than microorganisms can be easily multiplied.

The strenuous efforts of the laboratory worker to find a medium for pure culture studies seem to be provided in nature for many organisms. What appears laborious and complex to us in our artificial attempts is simple and direct as a natural process. Oftentimes associated products suggest the missing compound for pure culture operations, as has been experienced so often, but this frequently fails quantitatively or qualitatively through some neglected or undiscovered by-product.

In Pfeffer's disjunctive symbiosis many possibilities exist, but whether they may be regarded as a true biological association, or by analysis may be included in his conjunctive symbiosis, remains an open question.

Keeble's plant animals can be regarded as independent in a sense, but, on the other hand, they are very dependent. So too, the poled lima bean needs support which may in no manner be considered a part of its metabolism. For its best development the ivy needs a tree or stone wall; still, they are not biologically related. Because a streptococcus may accompany diphtheria infections and produce complications, or the tetanus organism is found in pyogenic processes, it does not follow that diphtheria is dependent upon streptococci or that the pyogenic organisms are dependent upon tetanus organisms, to appear in the pure individual life. That these processes may be modified or that these organisms of diphtheria and tetanus are perhaps fostered by association, will not be contradicted; yet they may live as independent forms. The pertinency of this class, therefore, must find its answer in physiological dependency or social independence with favoring or antagonistic elements.

If associations of microorganisms dependent or otherwise are subjected to analysis, there may be traced through them all some functional factor or principle as temperature, oxygen supply, food supply or condition of food (whether acid or alkaline, whether dry or moist, whether composed of one class of elements or another), or the production of metabolic products. For instance, the oxygen requirements may be illustrated by the growth of *Clostridium butyricum* in the presence of aerobic organisms; moisture by the elimination of many

[14] Keeble, F., "Plant-Animals—A Study of Symbiosis," Cambridge Press.

bacteria in a mixed culture composed of brine, and the persistence of cocci and torulæ; food by the feeding of ameba bacterially or acetic organisms with alcohol; reaction by the development of the lactic organisms in milk and the eradication of its associates; temperature by a combination in the growth of tubercle bacilli with saprophytes which will not grow at moderate temperature. Those fundamental biological requirements favor some forms of life association, while antagonizing others. Taken in conjunction with metabolic products as alcohol, lactic acid, acetic acid, amino-acids, ammonium, toxins and the many others that are possible, these biological factors offer a wide range of association, and at the same time determine the limitations.

Our experiences support these views, for involution forms or distorted morphology is easily traceable to one or more factors mentioned, and in the functioning processes of microorganisms how easy it is to alter the metabolic products and even the form by the addition or omission of an element. These acts have become an unconscious procedure and we do not, as a rule, make the subject one of systematic inquiry.

The association of animal and animal, or animal and plant, or plant and plant, when carried to comparatively loose social relations will in large part support this interpretation of these more intimate associations, illustrated through the channel of microorganisms. Animal life becomes adjusted to certain plants or other animal life, and is dependent upon their existence; plants depend upon animals and other plants; into which social relations enter the factors of food, temperature, and the other life conditions which apply to all living forms. Since this seems a fact so well established, and our work as microbiologists leads into the affairs of so many organisms which instigate numerous diverse changes—changes in some instances which are instituted by associational growth and which may affect their morphology, culture and physiology—it is pertinent in our researches to consider an organism in its natural microbial associations as significant as in a laboratory pure culture. Such factors should be directive for purposes of identification, study and application, since they suggest those possibilities which may be bound up in the intra- and inter-molecular relationships and reactions that dominate associations and individuals.

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Dr. A. F. A. King on Mosquitoes and Malaria[1]

Much as I might wish to write of Dr. King as a personal friend, as a great teacher, as a big, broad, warm-hearted human, in all of which rôles I knew him well, it has seemed best to your committee that I should confine my consideration to the single episode in the career of this many-sided man which relates to mosquitoes and malaria.

Dr. King was a deep thinker. He was not satisfied with even the generally accepted and apparently well founded views of men of science and of his own profession without a careful consideration and an ingenious twisting and testing of argument. This quality of mind he showed in a marked degree during the years 1881 and 1882 when he was filled with the thoughts of malaria and its probable origin and transmission. He never told me how or when the idea came to him that mosquitoes were transmitters of this disease. His search of the literature probably followed a fairly well worked out argument originating in his own mind. Surely he considered the idea as original when he came, probably late in 1881, to the laboratory of the late

[1] Read at the memorial meeting for Dr. A. F. A. King of the Medical Society of the District of Columbia, Washington, January 20, 1915.